UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,938	06/25/2001	Graham P. Allaway	50875-DA/JPW/SHS	9272

7590 05/31/2007

John P. White
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
PENG, BO	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
05/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/888,938	ALLAWAY ET AL.	
	Examiner	Art Unit	
	Bo Peng	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51 and 53-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51 and 53-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/15/07*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 15, 2007, has been entered.

2. This Office Action is in response to the amendment received on March 15, 2007. Claims 51 and 53-60 are pending and under examination in this Office action.

3. The rejection of Claims 51 and 53-58 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement **is withdrawn** in view of Applicant's argument.

4. The rejection of Claims 51 and 53-58 under the nonstatutory double patenting over Claims 1-5, 18 and 31 of Application No. 10/371,483 **is maintained**. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. Applicant acknowledges the rejection and does not wish to prematurely respond.

5. Following are new grounds of rejections:

Claim Rejections - 35 USC § 112, first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 57-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

8. Claims 57-60 are directed to a pharmaceutical composition comprising the antibody against CCR5 chemokine receptor, wherein the antibody is present in an amount effective to inhibit HIV-1 infection.

9. At the time the invention was made, it was known in the art that HIV-1 infects target cells via a chemokine receptor, such as CXCR4, on the surface of CD4 cells (Berger, 6,197,578). An antibody therapy against chemokine receptor for treating HIV infection was proposed (Berger, col. 16). However, no real medicine comprising antibodies against human chemokine receptor was tested for its clinical application for treating HIV infection. It is known in the art that a successful antibody therapy for treating viral infection *in vivo* is not routinely achievable by those skilled in the art. Most trials of antibody therapy for treating viral infection, such as for HAV, HBV and HIV infection, have been shown to have no treatment benefit, (Keller, 2000, Table 1, p. 606-607). Therefore, it is unpredictable in the art if the alleged pharmaceutical composition comprising anti-CCR5 antibodies can effectively inhibit HIV *in vivo*, resulting in treatment benefit.

10. The Court states that in order to provide proof of utility with regard to drugs and their

uses, either clinical, *in vivo* or *in vitro* data, or a combination of these can be used. However, the data must be such as to convince one of ordinary skill in the art that the proposed utility is sufficiently established. See in re Irons, 340 F. 2d 924,144 USPQ 351 (CCPA 1965), Ex parte Krepelka, 231 USPQ 746 (PTO Bd. Pat. App & Inter.1986) and Ex pane Chwang, 231 USPQ 751 (PTO Bd. Pat. App & Inter. 1986). In the instant case, the specification has not disclosed any specific anti-CCR5 antibody, or any real data, *in vitro* or *in vivo,* to show that the claimed antibody could be an effective medicine. Neither the specification nor the prior art has provided guidance or sufficient evidence that anti-CCR5 antibodies are enabling for treating HIV infection. Thus, a rationale to use pharmaceutical composition comprising CCR5 antibodies as a medicine for treating HIV infection *in vivo*, without presenting specific scientific data in the specification, is insufficient to convince one of ordinary skill in the art that the claimed pharmaceutical composition is effective for its intended use.

11. Since the pharmaceutical composition comprising CCR5 antibodies for treating HIV infection is not a conventional medicine known to one of ordinary skill in the art, one of ordinary skill in the art is unable to fully predict the possible properties or efficacy of the pharmaceuticals composition, therefore, clearly would not know how to use the asserted pharmaceutical composition comprising CCR5 antibodies for treating HIV infection without undue experimentation.

Claim Rejections - 35 USC § 102/103

12. Claims 51 and 53-56 are rejected under 35 U.S.C. § 102(e) as anticipated by, or in the alternative, under 35 U.S.C. § 103 as obvious over Li *et al.* (US 6,759,519), as evidenced by Wu

(US 6,528,265).

13. Claims 51 and 53-56 are directed to an isolated antibody which binds to a human CCR5 chemokine receptor on the surface of a CD4+ cell, wherein the antibody inhibits fusion of a HIV-1, or a HIV-1 infected cell, to the CD4+ cell, so as to thereby inhibit and inhibits HIV-1 infection of such CD4+ cell, wherein the CD4+ cell is a PM-1 cell, wherein the CD4+ cell is a primary CD4+ T-cell, wherein the CD4+ cell is a peripheral blood mononuclear cell (PBMC), wherein the antibody is a monoclonal antibody.

14. Li *et al.* disclose an antibody that binds the native HDGNR10 (Called CCR5 later) chemokine receptor polypeptide (SEQ ID NO: 2, Figure 1), which has an identical sequence to CCR5. Li teaches that said antibody is polyclonal, or monoclonal (col. 18 and claims). Li also teaches that an isolated antibody that binds a fragment, such as an extracellular portion, of HDGNR10. Li teaches that said antibody is an antagonist of the HDGNR10 polypeptide, which binds to the chemokine receptor but does not elicit a second messenger response such that the activity of the chemokine receptors is prevented (Line 19-27, col. 12).

15. Although Li does not explicitly teach that anti-HDGNR10 antibodies can block HIV utilizing CCR5 to enter CD4 cells, Li's antibodies should possess such property of blocking HIV fusion to CD4 cells because Li's polyclonal antibodies contain many antibodies that specifically bind to different epitopes of HDGNR10, at least one of which would be expected to have the claimed properties. Moreover, since Li teaches that an isolated antibody that binds an extracellular portion of HDGNR10, and said antibody is an antagonist of the HDGNR10 polypeptide, Li's antibody appears to have same characteristics of anti-CCR5 antibody that can block HIV fusion, as evidenced by Wu (6,528,625, cited in IDS). Wu teaches an anti-CCR5

antibody, mAb 2D7, which specifically binds to the second extracellular loop of CCR5 (L.51, col. 37), inhibits HIV entry (Figure 11), and also inhibits the chemotaxis of CCR5 in response to RANTES, MIP-1α and MIP-1β (L.60, col.38 to l. 23, col. 39, and Figure 10). Thus, the antibody of Li's (see especially Claim 21) should possess the functional characteristics recited in the pending claims. Therefore, the claimed antibodies appear to be the same or obvious variations of the antibodies disclosed in the prior art, absent a showing of unobvious differences.

16. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the antibodies of the prior art are not the same as the claimed antibodies. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed antibodies are different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 51 and 53-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cocchi *et al* (1995, Science Vol. 207, p.1811-1815, cited in IDS) and Samson *et al.* (1996, Biochemistry Vol. 35, p.3362-7, cited in IDS), both in view of Berger (US 6,197,578).

19. Claims 51 and 53-60 are directed to an isolated antibody which binds to a human

CCR5 chemokine receptor on the surface of a CD4+ cell, wherein the antibody inhibits fusion of a HIV-I, or a HIV-I infected cell, to the CD4+ cell, so as to thereby inhibit and inhibits HIV-I infection of such CD4+ cell, wherein the CD4+ cell is a PM-1 cell, wherein the CD4+ cell is a primary CD4+ T-cell, wherein the CD4+ cell is a peripheral blood mononuclear cell (PBMC), wherein the antibody is a monoclonal antibody; Claims 57-60 are directed to a pharmaceutical composition comprising the antibody against CCR5 chemokine receptor, wherein the antibody is present in an amount effective to inhibit HIV-1 infection.

20. Cocchi *et al.* teaches that the chemokines RANTES, MIP-1α, and MIP-1β were the major HIV suppressive factors to control HIV infection *in vivo* (whole document). Cocchi teaches that recombinant human RANTES, MIP-1α, and MIP-1β induce a dose-dependent inhibition of different strains of HIV-1, HIV-2, and SIV. Importantly, Cocchi teaches that antibodies against RANTES, MIP-1α, and MIP-1β can completely block the activity of the chemokines to block HIV infection.

21. Samson teaches that CCR5 (also called Chem R13) is a chemokine receptor, which can be stimulated by chemokines MIP-1α, MIP-1β and RANTES (Abstract, Para 2, left col. p.3393 and p. 3365-3367 and Figure 3). Samson also teaches the primary sequence and characterizes CCR5 structural feature of 7-transmembrane segment protein, like other G protein protein-coupled chemokine receptors (p. 3364 and Figure 1).

22. Neither Cocchi nor Samson teaches any antibody against CCR5 chemokine receptor that can inhibit HIV infection.

23. Berger teaches that one of the human chemokine receptors, CXCR4, on the surface of CD4+ cells is associated with HIV fusion (Figure 1). Berger teaches that the antibodies against

CXCR4 can block fusion of HIV to a CD4+ cell or an infected CD4 positive cell (col. 9-12; Example 2, col.20, and Figure 2). Berger also teaches specifically how to generate antibodies against chemokine receptors in Example 1 as recited: "Based on the known topology of 7-transmembrane segment proteins, four regions of CXCR4 are predicted to be exposed at the cell surface. Synthetic peptides are synthesized by methods well-known in the art that correspond to each of these 4 regions. Rabbit antisera is raised by immunization with peptide-KLH conjugates. Total immunoglobulin is purified from the preimmune and the immune sera by chromatographic separation with Protein-A Sepharose. Antibodies raised against the 38 amino acid N-terminal portion of CXCR4 blocked membrane fusion between the env-positive, LAV isolate of HIV-1, and CD4-positive, primary T cells. In contrast, antibodies raised against other peptide-KLH conjugates had no effect of membrane fusion between the virus and the target cells".

24. Berger also suggests the use of anti-CXCR4 chemokine receptor antibody as pharmaceutical compositions (col. 16) that block membrane fusion between HIV and a target cell.

25. It would have been obvious to the ordinary artisan at the time the invention was made to make antibodies against CCR5 in order to inhibit HIV fusion to CD4+ cells. The ordinary artisan would have been motivated to make these antibodies against CCR5 chemokine receptor and have a reasonable expectation of success, given the knowledge that the antibodies against chemokines RANTES, MIP-1α, and MIP-1β, can block HIV entry, as taught by Cocchi, given the knowledge that CCR5 is the receptor of chemokines RANTES, MIP-1α, and MIP-1β, as taught by Samson, and also given the knowledge that the antibody against CXCR4 chemokine receptor can block HIV fusion, as taught by Berger. On the analogy of anti-CXCR4 antibody, thus, one of ordinary

skill in the art would expect that an anti-CCR5 antibody that blocks CCR5 receptor should also block HIV entry CD4 cells via CCR5 chemokine receptor. Moreover, the CCR5 protein sequence was known at the time the invention was made, and its G protein protein-coupled receptor structural feature is characterized by Samson, one of ordinary skill in the art knows how to make an antibody against the chemokine receptor by routine experiments as taught by Berger. It is also within the level of ordinary skill to synthesize fragments of the antibody capable of binding to the chemokine receptor. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Remarks

26. No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The Examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, Ph. D. can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

BP
Bo Peng, Ph.D.
May 22, 2007

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600